## Remarks

Claims 1, 5, 6, 8, 12, 13, 15, 19, 20, 22, 26, 27, 29, 33 and 34 are pending.

Claims 7, 14, 21, 28 and 35 have been cancelled without prejudice. Applicants retain the right to divisional or continuation applications directed to the cancelled subject matter.

Claims 1, 8, 15, 22 and 29 have been amended and are supported by the specification at, for example, page 1, lines 16-19; page 5, lines 8-15; and page 57, lines 1-12.

Claims 6, 13, 20, 27 and 34 have been amended to delete "phenothiazine, a RGD peptide, a RDG peptide mimetic, an agent that blocks platelet glycoprotein IIb-IIIa receptors".

No issues of new mater should arise and entry of the amendment is respectfully requested.

# I. First Rejection under 35 U.S.C. §112, First Paragraph

Claims 1, 5-8, 12-15, 19-22, 26-29 and 33-35 are rejected under 35 USC § 112, first paragraph, as failing to comply with the written description requirement.

Applicants respectfully traverse the rejection and respectfully submit that the claims comply with the written description requirement.

As pointed out by the Examiner, the specification at pages 17-21 discloses S-nitroso-ACE inhibitors and the specification at page 23 discloses NO adducts having at least one -O-NO<sub>2</sub> group, wherein the NO adducts includes compounds, such as, for example, **polypeptides**. One skilled in the art knows that ACE inhibitors are polypeptides. Given the extensive disclosure for S-nitroso-ACE in the specification, at, for example, page 17, line 10 to page 21, line 15, it would be obvious for one skilled in the art on reading the specification to conclude that the NO adducts of the invention encompass ACE inhibitors (i.e. polypeptides) having at least one -O-NO<sub>2</sub> group.

In view thereof, Applicants respectfully submit that the claims satisfy the requirement under 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection under this provision be withdrawn.

# II. Second Rejection under 35 U.S.C. §112, First Paragraph

Claims 1, 5-8, 12-15, 19-22, 26-29 and 33-35 are rejected under 35 USC § 112, first paragraph, as lacking enablement.

Applicants respectfully traverse the rejection and respectfully submit that the claims are fully enabled.

As pointed out by the Examiner on page 3, of the Office Action, the specification is enabled for adverse effects associated with the use of medical devices in patients wherein the devices include nitric oxide adducts for local delivery at the site of contact of a device or instrument. In view of the amendment of the claims to recite "associated with the use of a medical device" the rejection is now moot.

In view thereof, Applicants respectfully submit that the claims satisfy the requirement under 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection under this provision be withdrawn.

#### III. Third Rejection under 35 U.S.C. §112, First Paragraph

Claims 5-7, 12-14, 18-21, 26-28 and 33-35 are rejected under 35 USC § 112, first paragraph, as lacking enablement.

Applicants respectfully traverse the rejection and respectfully submit that the claims are fully enabled.

In view of the amended to the claims to cancel "phenothiazine, a RGD peptide, a RDG peptide mimetic, an agent that blocks platelet glycoprotein IIb-IIIa receptors" and the therapeutic agents, the rejection is now moot.

In view thereof, Applicants respectfully submit that the claims satisfy the requirement under 35 U.S.C. § 112, first paragraph, and respectfully request that the rejection under this provision be withdrawn.

#### IV. Rejection under 35 U.S.C. §112, Second Paragraph

Claims 6-7, 13-14, 20-21, 27-28 and 34-35 are rejected under 35 USC § 112, first paragraph, as being indefinite.

Applicants respectfully traverse the rejection and respectfully submit that the claims satisfy the requirements under 35 U.S.C. § 112, second paragraph.

In view of the amended to the claims to cancel "a RGD peptide, a RDG peptide mimetic, an agent that blocks platelet glycoprotein IIb-IIIa receptors" and the therapeutic agents, the rejection is now moot.

In view thereof, Applicants respectfully submit that the claims satisfy the requirement under 35 U.S.C. § 112, second paragraph, and respectfully request that the rejection under this provision be withdrawn.

## V. First Rejection under 35 U.S.C. §102 (b)

Claims 1, 8, 15, 22 and 29 are rejected under 35 U.S.C. §102(b) as being anticipated by Loscalzo et al (U.S. Patent No. 5,025,001).

Applicants respectfully traverse the rejection and respectfully submit that the claims are not anticipated by Loscalzo. The Examiner has incorrectly stated that the compounds disclosed by Loscalzo and those of the present invention have the **same structure**. Loscalzo discloses angiotensin converting enzyme inhibitors that have at least one <u>-SNO group</u>. Loscalzo does not disclose or suggest angiotensin converting enzyme inhibitors that have at least one <u>-O-NO<sub>2</sub> group</u>. One skilled in the art readily knows that a <u>-SNO group</u> and a <u>-O-NO<sub>2</sub> group</u> are structurally different. Additionally Loscalzo does not provide any motivation for one to substitute the <u>-SNO group</u> with the <u>-O-NO<sub>2</sub> group</u> of the present invention. In fact nowhere in Loscalzo are <u>-O-NO<sub>2</sub> groups</u> even mentioned.

The compounds of the invention are **not disclosed** in Loscalzo, there is no motivation for one skilled in the art to use the claimed compounds based on the teachings in Loscalzo. Hence Loscalzo is non-analogous art and cannot form the basis of a rejection.

In view thereof, Applicants respectfully submit that the claims of the present invention are not anticipated by and are unobvious over Loscalzo, and respectfully request the rejection under 35 U.S.C. §102 be withdrawn.

#### VI. Second Rejection under 35 U.S.C. §102 (b)

Claims 1, 8, 15, 22 and 29 are rejected under 35 U.S.C. §102(b) as being anticipated by Loscalzo et al (U.S. Patent No. 5,002,964).

Applicants respectfully traverse the rejection and respectfully submit that the claims are not anticipated by Loscalzo. The Examiner has incorrectly stated that the compounds disclosed by Loscalzo and those of the present invention have the **same structure**. Loscalzo discloses angiotensin converting enzyme inhibitors that have at least one <u>-SNO group</u>. Loscalzo does not disclose or suggest angiotensin converting enzyme inhibitors which have at least one <u>-O-NO2 group</u>. One skilled in the art readily knows that a <u>-SNO group</u> and a <u>-O-NO2 group</u> are structurally different. Additionally Loscalzo does not provide any motivation for one to substitute the <u>-SNO group</u> with the <u>-O-NO2 group</u> of the present invention. In fact nowhere in Loscalzo are -O-NO2 groups even mentioned.

The compounds of the invention are **not disclosed** in Loscalzo, there is no motivation for one skilled in the art to use the claimed compounds based on the teachings in Loscalzo. Hence Loscalzo is non-analogous art and cannot form the basis of a rejection.

In view thereof, Applicants respectfully submit that the claims of the present invention are not anticipated by and are unobvious over Loscalzo, and respectfully request the rejection under 35 U.S.C. §102 be withdrawn.

## VII. Rejection under 35 U.S.C. §103

Claims 5-7, 12-14, 19-21, 26-28 and 33-35 are rejected under 35 U.S.C. §103 as being unpatentable over Loscalzo et al. (U. S. Patent No. 5,025,001) or Loscalzo et al (U. S. Patent No. 5,002,964) in view of Fuster et al.

Applicants respectfully traverse the rejection and respectfully submit that the claimed invention is unobvious over the cited references and there is no motivation to combine the cited references to arrive at the presently claimed invention. Applicants respectfully submit that the cited references, individually or in combination, do not disclose or suggest, or provide motivation to arrive at the presently claimed invention.

As mentioned above, Loscalzo (US '001 and US '964) do not disclose the compounds of the present invention. Additionally, as pointed out by the Examiner Loscalzo does not teach the administration of other active agents with the NO adducts. Hence Loscalzo, taken alone, does not render the claimed invention obvious.

Fuster does not cure the deficiencies of Loscalzo. Fuster does not provide any motivation or suggestion to modify Loscalzo to arrive at the claimed invention. In view thereof, Loscalzo in combination with Fuster does not motivate one to arrive at the present invention.

In view thereof, Applicants respectfully submit that the claims of the present invention are unobvious over the cited references, alone and in combination, and respectfully request the rejection under 35 U.S.C. §103(a) be withdrawn.

Amendment under 37 CFR § 1...1 Application No. 10/646,713 Page 9 of 9

# VIII. Conclusion

Applicants respectfully request reconsideration and allowance of claims 1, 5, 6, 8, 12, 13, 15, 19, 20, 22, 26, 27, 29, 33 and 34.

Examiner Ghali is encouraged to contact the undersigned concerning any questions about the present application.

Respectfully submitted,

Belief Len

Belinda M. Lew, Ph.D. Registration No. 53,212

Dated: October 24, 2006

Wilmer Cutler Pickering Hale and Dorr LLP

1875 Pennsylvania Avenue, NW

Washington, DC 20006 Phone: 202-663-6029